Amendment

In the Claims

1. (currently amended) A conjugate for use in targeting a drug to a tissue,

wherein the tissue overexpresses a digestive enzyme, the conjugate comprising: a polymeric carrier; a drug molecule; and a linker that includes a first end and a second end;

wherein the polymeric carrier is associated with the first end of the linker and the drug is associated with the second end of the linker,

wherein the polymeric carrier-conjugate is greater than about 6 nm in size, ~~and~~

wherein the linker includes an oligopeptide recognition segment that is cleaved when the conjugate is exposed to the digestive enzyme; and

wherein the digestive enzyme is selected from the group consisting of serine proteases and matrix metalloproteinases.

2. (currently amended) The conjugate of claim 1 further comprising: additional drug molecules; and additional linkers, wherein each drug molecule is indirectly associated with the polymeric carrier via one of the linkers and wherein each linker includes an oligopeptide recognition segment that is cleaved when the conjugate is exposed to the digestive enzyme.

3. (original) The conjugate of claim 1, wherein the polymeric carrier is hydrophilic, biocompatible and biodegradable.

4. (cancelled).

5. (original) The conjugate of claim 1, wherein the drug is a small molecule drug.

6. (original) The conjugate of claim 1, wherein the drug is a biomolecular drug.

7-8. (canceled).

9. (original) The conjugate of claim 1, wherein the tissue is diseased.

10. (original) The conjugate of claim 9, wherein the tissue is a tumor.

11. (original) A pharmaceutical composition comprising a pharmaceutically acceptable excipient and an effective amount of the conjugate of claim 1.

12. (currently amended) A method of preparing a conjugate for use in targeting a drug to a tissue, wherein the tissue overexpresses a digestive enzyme, the method comprising:

providing a polymer carrier; providing a drug molecule; providing a linker that includes at least a first end and a second end,

wherein the polymeric carrier-conjugate is greater than about 6 nm in size,

wherein the linker includes an oligopeptide recognition segment that is cleaved when the conjugate is exposed to the digestive enzyme, and the digestive enzyme is selected from the group consisting of serine proteases and matrix metalloproteinases;

associating the polymer carrier with the first end of the linker; and associating the drug molecule with the second end of the linker.

13. (currently amended) A method of administering a drug to a patient, the method comprising steps of:

providing a patient having a disorder characterized by the overexpression of a digestive enzyme;

administering to the patient a pharmaceutical composition that comprises a pharmaceutically acceptable excipient and an effective amount of a conjugate; and

administering the pharmaceutical composition to the patient; wherein the conjugate comprises:

a polymeric carrier; a drug molecule; and a linker that that includes a first end and a second end;

wherein the polymeric carrier-conjugate is greater than about 6 nm in size,

wherein the polymeric carrier is associated with the first end of the linker and the drug is associated with the second end of the linker;

wherein the linker includes an oligopeptide recognition segment that is cleaved when the conjugate is exposed to the digestive enzyme; and

wherein the digestive enzyme is selected from the group consisting of serine proteases and matrix metalloproteinases.

14. (previously presented) The conjugate of claim 1, wherein the polymeric carrier is dextran.

15. (currently amended) The conjugate of claim 1, wherein the oligopeptide recognition segment comprise the amino acid sequence IPVGLIG (SEQ ID NO:1).

16. (currently amended) The conjugate of claim 14, wherein the oligopeptide recognition segment comprise the amino acid sequence IPVGLIG (SEQ ID NO:1).

17. (previously presented) The conjugate of claim 1, wherein the drug is methotrexate.

18. (previously presented) The conjugate of claim 14, wherein the drug is methotrexate.

19. (previously presented) The conjugate of claim 15, wherein the drug is methotrexate.

20. (previously presented) The conjugate of claim 16, wherein the drug is methotrexate.

21. (previously presented) The conjugate of claim 1, wherein the drug is doxorubicin.

22. (previously presented) The conjugate of claim 14, wherein the drug is doxorubicin.

23. (currently amended) The conjugate of claim 22, wherein the oligopeptide recognition segment comprise the amino acid sequence IPVGLIG (SEQ ID NO:1).

24. (previously presented) The conjugate of claim 1, wherein the digestive enzyme is a serine protease.

25. (previously presented) The conjugate of claim 24, wherein the digestive enzyme is prostate specific antigen (PSA).

26. (previously presented) The conjugate of claim 24, wherein the digestive enzyme is human kallikrein 2 (hk2).

27. (previously presented) The conjugate of claim 24, wherein the digestive enzyme is urokinase-type plasminogen activator (uPA).

28. (previously presented) The conjugate of claim 24, wherein the digestive enzyme is fibroblast activating protein (FAP).

29. (previously presented) The conjugate of claim 1, wherein the digestive enzyme is a matrix metalloproteinase.

30. (previously presented) The conjugate of claim 29, wherein the digestive enzyme is Meprin.

31. (previously presented) The conjugate of claim 29, wherein the digestive enzyme is Meprin.

32. (previously presented) The conjugate of claim 29, wherein the digestive enzyme is MT1-MMP.

33. (previously presented) The conjugate of claim 29, wherein the digestive enzyme is matrix metalloproteinase II (MMP-2).

34. (previously presented) The method of claim 13, wherein the digestive enzyme is a serine protease.

35. (previously presented) The method of claim 34, wherein the digestive enzyme is prostate specific antigen (PSA).

36. (previously presented) The method of claim 34, wherein the digestive enzyme is human kallikrein 2 (hk2).

37. (previously presented) The method of claim 34, wherein the digestive enzyme is urokinase-type plasminogen activator (uPA).

38. (previously presented) The method of claim 34, wherein the digestive enzyme is fibroblast activating protein (FAP).

39. (previously presented) The method of claim 13, wherein the digestive enzyme is a matrix metalloproteinase.

40. (previously presented) The method of claim 39, wherein the digestive enzyme is Meprin.

41. (previously presented) The method of claim 39, wherein the digestive enzyme is Meprin.

42. (previously presented) The method of claim 39, wherein the digestive enzyme is MT1-MMP.

43. (previously presented) The method of claim 39, wherein the digestive enzyme is matrix metalloproteinase II (MMP-2).

44. (previously presented) The method of claim 13, wherein the polymeric carrier is dextran.

45. (currently amended) The method of claim 13, wherein the oligopeptide recognition segment comprise the amino acid sequence IPVGLIG (SEQ ID NO1:).

46. (currently amended) The method of claim 44, wherein the oligopeptide recognition segment comprise the amino acid sequence IPVGLIG (SEQ ID NO:1).

47. (previously presented) The method of claim 13, wherein the drug is methotrexate.

48. (previously presented) The method of claim 44, wherein the drug is methotrexate.

49. (previously presented) The method of claim 45, wherein the drug is methotrexate.

50. (previously presented) The method of claim 46, wherein the drug is methotrexate.

51. (previously presented) The method of claim 13, wherein the drug is doxorubicin.

52. (previously presented) The method of claim 44, wherein the drug is doxorubicin.

53. (currently amended) The method of claim 52, wherein the oligopeptide recognition segment comprise the amino acid sequence IPVGLIG (SEQ ID NO:1) .

54. (previously presented) The method of claim 13, wherein the conjugate is administered in an amount effective to treat an epithelial cancer in the patient.

55. (previously presented) The method of claim 13, wherein the conjugate is administered in an amount effective to treat breast, prostate, bladder, ovarian, bladder, or gastric cancer in the patient.

56. (previously presented) The method of claim 13, wherein the conjugate is administered in an amount effective to treat arthritis in the patient.